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Amendments to the Claims

This listing of claims will replace all prior versions, and
listings, of claims in the application:

Listing of Claims

1-157. (Canceled)

158. (Currently Amended) A method for identifying a protein target as being able to bind a ligand, comprising:

- (a) providing a molecule comprising a methotrexate moiety covalently linked to the ligand, which methotrexate moiety binds to a dihydrofolate reductase;
- (b) introducing the molecule into a cell which i) expresses a first fusion protein comprising the dihydrofolate reductase capable of binding that binds to the methotrexate moiety, ii) expresses a second fusion protein comprising the protein target, wherein either the first or second fusion protein also comprises a transcription activator domain and the other fusion protein comprises a DNA-binding domain, and iii) has a reporter gene, wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein and wherein the DNA-binding domain binds upstream of the reporter gene, and wherein the cell is a yeast cell;
- (c) permitting the molecule to bind to the first fusion protein and to the second fusion protein so as to activate the expression of the reporter gene; and

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(d) selecting the cell if it expresses the reporter gene, so as to thereby identify the protein target as being able to bind the ligand.

159. (Previously Presented) The method of claim 158, wherein the protein target is encoded by genomic DNA or a cDNA.

160. (Cancelled)

161. (Currently Amended) The method of claim 158, wherein the first fusion protein is ~~(dihydrofolate reductase)~~ (dihydrofolate reductase)-(DNA-binding domain).

162. (Currently Amended) The method of claim 158, wherein the first fusion protein is ~~(dihydrofolate reductase)~~ (dihydrofolate reductase)-(LexA).

163. (Currently Amended) The method of claim 158, wherein the first fusion protein is ~~(dihydrofolate reductase)~~ (dihydrofolate reductase)-(transcription activation domain).

164. (Currently Amended) The method of claim 158, wherein the first fusion protein is ~~(dihydrofolate reductase)~~ (dihydrofolate reductase)-(B42).

165. (Currently Amended) The method of claim 158, wherein the second fusion protein comprises a DNA-binding domain.

166. (Previously Presented) The method of claim 158, wherein the second fusion protein comprises LexA.

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167. (Previously Presented) The method of claim 158, wherein the second fusion protein comprises a transcription activation domain.

168. (Previously Presented) The method of claim 158, wherein the second fusion protein comprises B42.

169. (Currently Amended) The method of claim 158, wherein the cell is S. cerevisiae or E. coli Sacchromyces cerevisiae.

170. (Previously Presented) The method of claim 158, wherein the reporter gene is lacZ, Gal4 or Ura-3.

171. (Currently Amended) The method of claim 158, wherein the cell is a bacterial cell, the molecule comprises a methotrexate moiety bound to the ligand, the first fusion protein comprises a dihydrofolate reductase and a LexA, the second fusion protein comprises the protein target and B42, and the reporter gene is LacZ.

172. (Currently Amended) The method of claim 158, wherein the cell is a yeast cell, the molecule comprises a methotrexate moiety bound to the ligand, the first fusion protein comprises a dihydrofolate reductase and a LexA, the second fusion protein comprises the protein target and B42, and the reporter gene is Gal4.

173-180. (Cancelled)

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181. (New) A method for identifying a protein target as being able to bind a ligand, comprising:

- (a) providing a molecule comprising a methotrexate moiety covalently linked to the ligand, which methotrexate moiety binds to a dihydrofolate reductase;
- (b) introducing the molecule into a cell which i) expresses a first fusion protein comprising the dihydrofolate reductase that binds to the methotrexate moiety, ii) expresses a second fusion protein comprising the protein target, wherein either the first or second fusion protein also comprises a transcription activator domain and the other fusion protein comprises a DNA-binding domain, and iii) has a reporter gene, wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein and wherein the DNA-binding domain binds upstream of the reporter gene, and wherein the cell is a bacterial cell;
- (c) permitting the molecule to bind to the first fusion protein and to the second fusion protein so as to activate the expression of the reporter gene; and
- (d) selecting the cell if it expresses the reporter gene, so as to thereby identify the protein target as being able to bind the ligand.

182. (New) The method of claim 181, wherein the protein target is encoded by genomic DNA or a cDNA.

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183. (New) The method of claim 181, wherein the first fusion protein is (dihydrofolate reductase)-(DNA-binding domain).

184. (New) The method of claim 181, wherein the first fusion protein is (dihydrofolate reductase)-(LexA).

185. (New) The method of claim 181, wherein the first fusion protein is (dihydrofolate reductase)-(transcription activation domain).

186. (New) The method of claim 181, wherein the first fusion protein is (dihydrofolate reductase)-(B42).

187. (New) The method of claim 181, wherein the second fusion protein comprises a DNA-binding domain.

188. (New) The method of claim 181, wherein the second fusion protein comprises LexA.

189. (New) The method of claim 181, wherein the second fusion protein comprises a transcription activation domain.

190. (New) The method of claim 181, wherein the second fusion protein comprises B42.

191. (New) The method of claim 181, wherein the cell is *Escherichia coli*.

192. (New) The method of claim 181, wherein the reporter gene is lacZ, Gal4 or Ura-3.

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193. (New) The method of claim 181, wherein the molecule comprises a methotrexate moiety bound to the ligand, the first fusion protein comprises a dihydrofolate reductase and a LexA, the second fusion protein comprises the protein target and B42, and the reporter gene is LacZ.

194. (New) The method of claim 181, wherein the molecule comprises a methotrexate moiety bound to the ligand, the first fusion protein comprises a dihydrofolate reductase and a LexA, the second fusion protein comprises the protein target and B42, and the reporter gene is Gal4.